Medical Treatment versus Prevention of Peptic Ulcer*

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THE present handling of the problem of peptic ulcer is unsatisfactory. This is attested by the eagerness with which both physicians and victims of the disease greet the announcement of every newly proposed remedy. In order to avoid confusion and to appraise this problem in the proper perspective it is necessary to distinguish between the treatment of the individual acute ulcer episode and the measures designed to combat the tendency to recurrent ulcers.

The present methods for treatment of uncomplicated ulcer as used in the leading clinics are effective in producing prompt relief and in healing the ulcer in a matter of weeks in over 90 per cent of the cases. For this reason there is no room for radical improvement so far as results of treatment in the individual attack of ulcer are concerned. When difficulties arise it is usually from failure to apply the well known methods of therapy on the part of the physician or from lack of cooperation on the part of the patient.

The therapeutic research in peptic ulcer during the past two decades has dealt chiefly with new antacid remedies (magnesium trisilicate, aluminum hydroxide and phosphate, polyamine-formaldehyde resin), with biological products which reduce gastric secretion (enterogastrone and urogastrone), with substances which counteract peptic activity (saponins), and with substitutes of milk for frequent feedings (milk tablets, gelatin, amino-acids†). These efforts are very welcome because their results contribute to the more efficient therapy of some cases of ulcer that are "intractable" on the classical regimen and because some of them obviate certain inconveniences of this regimen to patients during the early weeks of treatment. On the other hand, their importance is limited by the facts that less than 10 per cent of uncomplicated cases of peptic ulcer are "intractable" and that it is not inconvenience of the treatment that gives rise to the general dissatisfaction. It must be clearly understood that none of the old or new therapeutic methods employed in medicine go beyond the treatment of the current ulcer episode, with the possible exception of an as yet unidentified experimental substance contained in "enterogastrone-concentrate" described by Greengard, Atkinson, Grossman and Ivy. Surgical operations for treatment and prevention of peptic ulcer are discussed in another paper of this panel discussion.

The classical ulcer treatment was originated by Sippy in 1912. Three years later his first results were published, indicating successful healing of the ulcer in 85 per cent of cases. Since then various relatively unimportant modifications of this treatment have been introduced. The most significant of these is the use of insoluble or relatively insoluble antacids. The routine treatment of uncomplicated peptic ulcer at the University of California Gastro-intestinal Clinic is carried out under ambulatory conditions. During the first week the diet is limited to a milk and cream mixture taken every two hours with antacid powders one hour after the mixture. Sedative and antispasmodic medication is administered three times a day. During the second week this schedule is continued with the addition of certain foods only if complete relief from pain has been achieved during the first week. These additions consist of eggs, cottage cheese, white bread, potatoes, macaroni, rice, oatmeal and cream of wheat at meal times. Sugar, salt and butter are also allowed. During the first two weeks of treatment great emphasis is placed on the regularity of food intake and antacid medication (not more than five minutes before or after the hour). Beginning with the third week, cooked fruits and pureed vegetables are added and the punctuality of the schedule is relaxed. Gradual additions to the diet are made with less frequent administration of milk until, in the average case, the patient is on a general diet three months after beginning of treatment. All medication is carried out for at least four months and antacids are continued for at least six months from beginning of treatment.

If complete relief from pain is not obtained during the first week, rest from work, bed rest at home or in the hospital, nocturnal intragastric drip of aluminum hydroxide (Winkelstein), and psychotherapy are prescribed as dictated by circumstances.

There is an unfortunate tendency among many physicians to think that the described or kindred modification of the Sippy diet are too strict to be practical for most of their patients with peptic ulcer. This is true even of some of those who had opportunity to observe the excellent immediate results of this type of treatment in their senior year in medical school and during their internship. As a result compromises are made going all the way to the vague advice to "drink a lot of milk" and the administration of antacids limited to three times a day. In the first place, such compromises increase the number of patients who fail to respond to medical therapy. These patients, are, therefore, labeled "intractable" and subjected to surgical operations. In the second place, inadequate treatment may bring about a state in which the patient loses his pain entirely or partially while activity in the ulcer continues in a latent form.

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† Essentially predigested milk protein.

This is especially true of individuals who are hyposensitive to pain. Crohn has shown that the proportion of such individuals among patients with peptic ulcer is about three times greater than in the general population, so that this characteristic applies to a majority of ulcer patients. It is difficult to determine exactly how often such a state of latent activity occurs in a given series of patients under treatment. Frequent roentgenologic checks are helpful, but not altogether conclusive and, unfortunately, expensive. Probably the most generally applicable criterion of the incidence of latent activity in ulcers under treatment is the number of patients experiencing a return of pain during the later stages of the ulcer regimen or soon after cessation of treatment in the absence of known "inciting" causes of recurrences. Such patients are often classified as having "spontaneous" recurrences.

The tendency of patients who have had one episode of peptic ulcer to have subsequent episodes is very great. Eusterman and Balfour observed among private patients at the Mayo Clinic that five-year cures were obtained in about 50 per cent of cases "provided that the conditions were favorable and the therapeutic regime adequate." St. John and Flood reported a recurrence rate of 65 per cent among clinic patients in New York who were followed for two years. This rose to 78 per cent in their patients who were followed for five years. Crohn reported recurrences of peptic ulcer among "about 60 per cent" of his ward hospital patients in five years and among "over 70 per cent" of them in ten years. Bockus, speaking of a private practice, stated that he had less than 10 per cent of recurrences in six months and 50 per cent of recurrences in five years "unless special care was taken." Raimondi and Collen reported that in an industrial contract practice they observed 66 per cent of recurrences in one year and 83 per cent of recurrences in two years. From the data supplied by Holland and Logan on recurrences of peptic ulcer in patients followed for up to 20 years, it appears that, when patients with gastric ulcer remained free from recurrences for five years, they could be considered as virtually cured. On the contrary, patients with duodenal ulcer were subject to recurrences even after having remained well for periods between 15 and 20 years.

From these figures and the excellent immediate results with medical therapy it is clear that the chief unsolved problem confronting the medical profession in connection with peptic ulcer in general, and the much more common duodenal ulcer in particular, is not the healing of the current ulcer episode but the prevention of recurrences. This is true regardless of the type of medical practice, whether private, clinic or contract. The rate of recurrences of peptic ulcer seems to be somewhat lower in private patients, but it is difficult to say whether this is due to a greater ability or willingness to observe precautions on the part of this class of patient, or to better opportunities of consulting different physicians for subsequent recurrences.

Before discussing a program for the prevention of ulcer recurrences it is necessary for purposes of orientation to review the chief known "inciting" causes of such recurrences. From the figures furnished by Emery and Monroe's follow-up study of 1,279 patients with recurrent peptic ulcer, it can be calculated that, of the recurrences for which a cause could be assigned, 42 per cent were due to fatigue, 32 per cent to emotional disturbances, 21 per cent to infections predominantly of the upper respiratory tract, and 5 per cent to indiscretion in diet. From a similar study of 350 patients, Jankelson found that relapses were caused by: dietary errors, 30 per cent; mental or physical strain, 24 per cent; seasonal, 19 per cent; infections, 15 per cent; drugs, 2 per cent; trauma, 1 per cent; unclassified, 9 per cent.

INCITING CAUSES OF RECURRENCES

From these data which are supported by the experience of every physician dealing with peptic ulcer patients, it is clear that the important known "inciting" causes of recurrences are: physical or mental fatigue, emotional disturbances, dietary indiscretions, and respiratory infections. In dealing with the causes of ulcer recurrences from the prophylactic point of view, it is obvious that at present the only practical medical approach is education of the patient. It is here that the physician often fails the patient by neglecting to inform him of the true nature and probable future course of his disease if proper precautions are not observed indefinitely.

Before embarking on such a far reaching educational campaign, it is essential in each case to establish firmly the diagnosis of peptic ulcer in order not to place an unfair burden on the patient and, as a secondary consideration, not to waste the physician's time. The diagnosis of peptic ulcer should not be lightly made, and preferably positive roentgenologic evidence should be obtained in each case. Least of all should the term "ulcers" be used as a cliche to satisfy an inquisitive patient with indigestion of undetermined origin. Also excessive reliance should not be placed on the roentgenologic examination alone, especially if it is not performed by a competent full-time radiologist. Old scarring of the duodenum, coarse rugae or extrinsic pressure may produce a roentgenologic appearance suggestive of ulcer. Correlation with the psychic make-up of the patient, the clinical history and the physical examination—especially the presence of a sharply circumscribed tenderness over the duodenum—is very important.

In dealing with ulcer patients and especially in trying to persuade them to observe certain precautionary measures for a period of many years, if not for the rest of their lives, it is necessary to take into account their personality. The typical patient with a peptic ulcer is a tense, ambitious, meticulous, overconscientious person who minimizes his pain, in contrast to the usual psychoneurotic or hypochondriac patient who habitually exaggerates his symptoms. The ulcer patient often neglects his treatment because it interferes with his work, unless the physician makes a determined effort to enlist the patient's cooperation by explaining to him the essentials of the ulcer prob-

lem. After this is done many patients are converted to a meticulous observance, not only of the immediate therapeutic regimen, but also of the long range prophylactic measures. It is also worthy of note that the tensions of most ulcer patients, as is pointed out by Lion, are associated with an occupational predicament or, less frequently, with other objective difficulties of a domestic or financial nature. For this reason the physician should inform himself particularly about the nature of the patient's work, his ambitions, his working hours and surroundings, how his evenings and week-ends are spent, whether the patient takes any vacations and what he does with them. The family relations, financial affairs, and any other matters which may be close to the patient's heart should be explored for possible sources of tension.

At the time the diagnosis is discussed with an often over-anxious patient it may be necessary to reassure him, especially if he fears that the ulcer "will turn into a cancer." Since the large majority of peptic ulcers are duodenal in location, fortunately one can be very emphatic in denying this possibility in these cases. To patients with gastric ulcers the precautions to rule out the threat of cancer by repeated roentgenologic examination should be explained. Later the patient must be informed frankly that peptic ulcer is, as so well defined by Jones, "a chronic, incurable disease characterized by ulceration of the stomach or duodenum and subject to intermittent relief from symptoms, as well as to unpredictable, or frequently predictable recurrences. A condition which, while capable of being handled during acute phases, does not respond to treatment in such a manner as to provide a complete and lasting cure. Complete cures . . . are the rare exception; recurrences are the rule."

Having imparted to the patient a general understanding of the problem of peptic ulcer, including a brief mention of the common complications of stenosis, hemorrhage and perforation, the physician can proceed to a discussion of practical preventive measures as they apply to the individual circumstances of the case. The patient's work predicament, if any, is discussed and its importance pointed out. It is often possible for the physician to make constructive suggestions on how to lighten the occupational burden. In extreme cases a change of occupation may have to be advised. Emotional disturbances involving family or financial matters or other frustrations should be tactfully inquired into. If such troubles are present, an effort should be made to solve them, or, when this is impossible, an attempt should be made to inculcate in the patient a more detached attitude toward his difficulties. In major cases it is necessary to enlist the services of a psychiatrist. The importance of moderation in eating is then taken up. The strictness of instructions in this direction depends on the amount of permanent scarring in the duodenum, on the degree of residual hyperacidity and hypermotility, and on the estimate of the patient's tendency to discount medical advice. It is of great advantage if the patient can be induced to abandon the use of coffee, tobacco and alcohol. However, compromises in these respects are often advisable, lest by insisting on excessively strict measures (from the patient point of view), he is prejudiced against the whole program of preventing recurrences. Finally the patient should be impressed with the importance of taking care of colds. Most important are regular measurements of temperature during respiratory infections with bed rest for the duration of the febrile period if any, and warning against excessive use of medication containing aspirin.

During periods of unavoidable fatigue or emotional stress the patient must be instructed to go on a protective diet eliminating coarse and irritating foods, and to resume medication with antacid, antispasmodic and sedative preparations of which he should keep a supply at home for such contingency. In addition to these precautions the patient should be prepared to handle any recurrence of ulcer pain by going promptly on the first stage of the strict ulcer diet and reporting at once to his physician. In case of rapid disappearance of symptoms an abbreviated course of treatment limited to one month is permissible at the discretion of the physician.

The instruction of the patient regarding the nature of his disease and the "inciting" causes of recurrences should be carried out systematically during each visit and summarized at the time of discharge from the care of his physician. In addition it is a good practice to supply the patient with a printed list of precautions which he is to read over once a month.

SUMMARY

1. *Adequate* medical treatment of uncomplicated peptic ulcer produces prompt relief and early healing of the current ulcer in over 90 per cent of cases.

2. Failure of the physician to insist on a strict and sustained regimen decreases the percentage of successful cases and results in early recurrences.

3. Medical treatment, *per se*, at present contributes nothing toward prevention of recurrences which are so frequent in all types of medical practice that, with few exceptions, peptic ulcer should be considered an incurable disease which must be kept under control by appropriate measures.

4. Recurrences of peptic ulcer are associated with four main "inciting" causes: Physical and mental fatigue, emotional disturbances, dietary indiscretions and respiratory infections.

5. In addition to prescribing an adequate regimen, the physician has a threefold duty toward the ulcer patient: to instruct him in the true nature of his disease, to convince him of the necessity of long continued preventive measures, and to assist him in readjusting his life for the purpose of avoiding tension.

6. In the event of recurrence of ulcer pain the patient should be prepared to resume at once the strict diet and medications, and report to his physician.

QUESTIONS AND ANSWERS

DR. ALTHAUSEN: The first question asks for comment on protein hydrolysate in the treatment of peptic ulcer.

Protein hydrolysate is essentially pre-digested milk pro-

tein, only in more concentrated form. For that reason it has certain advantages when the patient is in a poor stage of nutrition, because it provides him with more protein, especially during the first week. However, it cannot be used for patients who are allergically sensitive to milk, because they are also allergically sensitive to the casein hydrolysate, since the hydrolysis is never complete.

The second question is: "In your experience, do intramuscular injections of liver extract increase the amount of red cells following hemorrhage?"

I think if we are dealing with large hemorrhage, the blood should be replaced by transfusion. If there is continuous bleeding in small amounts over a long period of time, then liver extracts, together with iron—I should place iron first in importance—would be advantageous. On the other hand, in a single hemorrhage, which is not too great, I think the patients recover just about as rapidly without supplementary treatment, such as liver extract and iron, as with such treatment.

The next question is: "Would a daily use of amino acids in milk tend to prevent a recurrence?"

Amino acids in milk are sometimes given, but in ordinary interval feedings I do not think it would be necessary. Plain milk would probably serve the same purpose. On the other hand, it is rather difficult to get patients who have no symptoms to adhere to a five or six meal regime. The whole difficulty with patients who have recurring ulcers is that they are often not willing to observe precautions when they are free of symptoms. There is something in them that rebels against treating themselves as invalids.

The next question is: "Do you place patients with 'duodenitis' or 'duodenal erosions' in the same category as those with a solitary peptic ulcer in regard to treatment and etiology?"

Yes. I think that people with duodenitis, who can be defined as patients who have essentially the ulcer type of symptoms but during an x-ray examination show irritation of the duodenal caps rather than any direct or indirect evidence of ulcer, belong in the peptic ulcer category, but have not progressed as far on the road to ulcer as patients who have a frank ulcer. They usually have hypersecretion of gastric acid, and the same emotional problems or overwork. So the treatment is the same as for frank ulcer, and it is very effective. However, I don't try to educate these patients as rigidly as I do patients with actual ulcer. Individuals do not develop an ulcer, no matter what their physical or psychological state, unless they have some unknown predisposing factor. I think that people with duodenitis have this "X" factor to a lesser degree, because I have followed a number of patients with duodenitis for some ten or fifteen years, without their ever developing an actual ulcer demonstrable roentgenographically.

One of my patients with duodenitis was assigned during the war to a little tanker that supplied gasoline to outlying Navy bases in the Pacific. This tanker was not considered of sufficient importance to be provided with a destroyer escort so it went unescorted into Japanese-infested waters, and on several occasions was shelled by enemy submarines. My patient had a recurrence of his duodenitis but even under these conditions, he did not develop an actual ulcer.

Another question is: "What is your explanation of the lifelong recurrences of duodenal ulcers in contrast to the relatively few recurrences of gastric ulcer after a five-year cure?"

I don't know. We see very few gastric ulcers, and I was interested in the statistics published by Holland and Logan. Perhaps Dr. Snell could shed some light on this question.

The last question is: "Do you believe an injection treatment for ulcer to be of any value, other than psychological? If not, is it justified in any case? If so, why not give plain saline, which would be cheaper?"

I suppose this refers particularly to the injection of histidine monohydrochloride, which was advocated at one time for the treatment of peptic ulcer. One member of our staff tried it about 12 or 15 years ago on a series of patients, and found that the percentage of failures was very much greater than with the standard type of medical treatment.

Greengard et al. are working on an as yet unidentified substance contained in "enterogastrone-concentrate" which is given by injection and they have reported favorable results in the treatment of peptic ulcer. At present this treatment is still in the experimental stage. It requires several injections a week which are apt to be painful so that the place of injection has to be changed frequently. These workers had no recurrences during a limited period of observation but the treatment is more drastic than observing some of the precautions I tried to indicate here this morning.

MODERATOR SNELL: Thank you, Dr. Althausen. I regret that I can cast no light on the question of why there are more five-year cures in gastric ulcers than there are in duodenal ulcers. Perhaps benign gastric ulcer is a psychic phenomena, a periodic disease.

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